Notice of Allowability	Application No.	Applicant(s)	
	09/880,107	HORNE ET AL.	
	Examiner	Art Unit	
	Jehanne S Sitton	1634	
The MAILING DATE of this communication appe All claims being allowable, PROSECUTION ON THE MERITS IS (herewith (or previously mailed), a Notice of Allowance (PTOL-85) NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIG	(OR REMAINS) CLOSED in or other appropriate commits. This application is and MPEP 1308.	n this application. If not included unication will be mailed in due course. THIS	S ative
1. This communication is responsive to the paper mailed April	<u>1 20, 2004</u> .		
2. The allowed claim(s) is/are <u>5-7,9-11,13,49-53,55 and 57-61</u>	<u>l</u> .		
3. The drawings filed on <u>14 June 2001</u> are accepted by the Ex	kaminer.		
 4. ☐ Acknowledgment is made of a claim for foreign priority un a) ☐ All b) ☐ Some* c) ☐ None of the: 1. ☐ Certified copies of the priority documents have 		or (f).	
2. Certified copies of the priority documents have	been received in Applicati	on No	
Copies of the certified copies of the priority doc	cuments have been receive	d in this national stage application from the	
International Bureau (PCT Rule 17.2(a)).		·	
* Certified copies not received:			
Applicant has THREE MONTHS FROM THE "MAILING DATE" of noted below. Failure to timely comply will result in ABANDONM THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.	of this communication to fill ENT of this application.	e a reply complying with the requirements	
5. A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.			
6. CORRECTED DRAWINGS (as "replacement sheets") must be submitted.			
(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached			
1) hereto or 2) to Paper No./Mail Date			
(b) ☐ including changes required by the attached Examiner's Paper No./Mail Date	Amendment / Comment o	r in the Office action of	
Identifying indicia such as the application number (see 37 CFR 1. each sheet. Replacement sheet(s) should be labeled as such in the	84(c)) should be written on the header according to 37 C	he drawings in the front (not the back) of FR 1.121(d).	
7. DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.			
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Attachment(s) 1. ☐ Notice of References Cited (PTO-892)	E □ Nation of I	oformal Patent Application (PTO-152)	
2. Notice of Draftperson's Patent Drawing Review (PTO-948)	<u>=</u>	ummary (PTO-413),	
	Paper No.	/Mail Date	
3. Information Disclosure Statements (PTO-1449 or PTO/SB/08 Paper No./Mail Date	_	Amendment/Comment	
 Examiner's Comment Regarding Requirement for Deposit of Biological Material 	8. ☐ Examiner's 9. ☐ Other	Statement of Reasons for Allowance	
•		_ ·	
JEHANNE SITTON PRIMARY EXAMINE 9 Chames 211/05	# #~		

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Michael Tuscan on February 1, 2005.

The application has been amended as follows:

Please cancel claims 47 and 48.

Claim 5. (Currently amended) A method of diagnosing hepatocellular carcinoma in a human patient, comprising:

(a) detecting the level of expression in a tissue sample of [two] <u>ten</u> or more genes from Tables 3A, 3B, 5, 7A, 7B, 8A, and 8B; wherein differential expression of the genes in Tables 3A, 3B, 5, 7A, 7B, 8A, and 8B is indicative of hepatocellular carcinoma.

Claim 6. (Currently amended) A method of detecting the progression of hepatocellular carcinoma in a human patient, comprising:

(a) detecting the level of expression in a tissue sample of [two] ten or more genes from Tables 3A, 3B, 5, 7A, 7B, 8A, and 8B; wherein differential expression of the genes in Tables 3A, 3B, 5, 7A, 7B, 8A, and 8B is indicative of hepatocellular carcinoma progression.

Claim 7. (Currently amended) A method of monitoring the treatment of a human patient with hepatocellular carcinoma, comprising:

- (a) administering a pharmaceutical composition to the patient;
- (b) detecting the level of expression of ten or more genes from Tables 3A, 3B, 5, 7A, 7B, 8A and 8B [preparing a gene expression profile] from a cell or tissue sample from the patient; and
- (c) comparing the patient gene expression [profile] <u>detected in step (b)</u> to [a] gene expression from a cell population comprising normal liver cells or to [a] gene expression [profile] from a cell population comprising hepatocellular carcinoma cells or both.
- Claim 9. (Currently amended) A method of diagnosing a metastatic liver cancer in a human patient, comprising:
- (a) detecting the level of expression in a tissue sample of [two] <u>ten</u> or more genes from Tables 4A, 4B, 5, 6A, 6B, 9A and 9B; wherein differential expression of the genes in Tables 4A, 4B, 5, 6A, 6B, 9A, and 9B is indicative of metastatic liver cancer.
- Claim 10. (Currently amended) A method of detecting the progression of a metastatic liver cancer in a human patient, comprising:
- (a) detecting the level of expression in a tissue sample of [two] <u>ten</u> or more genes from Tables 4A, 4B, 5, 6A, 6B, 9A and 9B; wherein differential expression of the genes in Tables 4A, 4B, 5, 6A, 6B, 9A, and 9B is indicative of metastatic liver cancer progression.

Claim 11. (Currently Amended) A method of monitoring the treatment of a human patient with metastatic liver cancer, comprising:

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- (a) administering a pharmaceutical composition to the patient;
- (b) detecting the level of expression of ten or more genes from Tables 4A, 4B, 5, 6A, 6B, 9A and 9B [preparing a gene expression profile] from a cell or tissue sample from the patient; and
- (c) comparing the patient gene expression [profile] detected in step (b) to [a] gene expression from a cell population comprising normal liver cells or to [a] gene expression [profile] from a cell population comprising metastatic liver tumor cells or both.
- Claim 13. (Currently amended) A method of differentiating metastatic liver cancer from hepatocellular carcinoma in a human patient, comprising:
- (a) detecting the level of expression in a tissue sample of [two] <u>ten</u> or more genes from Tables 3-9; wherein differential expression of the genes in Tables 3-9 is indicative of metastatic liver cancer rather than hepatocellular carcinoma.
- Claim 51. (Currently Amended) A method of diagnosing hepatocellular carcinoma or metastatic liver cancer in a human patient comprising:
- (a) [preparing a gene expression profile] detecting the level of expression of ten or more genes from Tables 3-9 from a tissue sample from the patient; and

(b) comparing the gene expression [profile] detected in step (a) to a database comprising

part of the data in Tables 3-9; wherein differential expression of the genes detected in step (a) is

indicative of hepatocellular carcinoma or metastatic liver cancer.

Claim 58. (Currently Amended) A method of diagnosing hepatocellular carcinoma in a human

patient, comprising:

(a) detecting the level of expression in a liver tissue sample of [two] ten or more mRNA

species from Table 3A, 3B, 5, 7A, 7B, 8A or 8B; and

(b) comparing the detected level of expression to the level of expression of said [two] ten

or more mRNA species in a hepatocellular carcinoma liver tissue sample, thereby diagnosing

hepatocellular carcinoma in the patient.

Claim 59. (Currently Amended) A method of diagnosing metastatic liver cancer in a human

patient, comprising:

(a) detecting the level of expression in a liver tissue sample of [two] ten or more mRNA

species from Table 4A, 4B, 5, 6A, 6B, 9A or 9B; and

(b) comparing the detected level of expression to the level of expression of said [two] ten

or more mRNA species in a metastatic liver cancer tissue sample, thereby diagnosing metastatic

liver cancer in the patient.

Claim 60. (Currently Amended) A method of claim 58, wherein the level of expression of said [2] ten or more mRNA species in a hepatocellular carcinoma liver sample is in Table 3A, 3B, 5, 7A, 7B, 8A or 8B.

Claim 61. (Currently Amended) A method of claim 59, wherein the level of expression of said [2] ten or more mRNA species in a metastatic liver cancer sample is in Table 4A, 4B, 5, 6A, 6B, 9A or 9B.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton

Primary Examiner
Art Unit 1634

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